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NEW METHODS FOR CALCULATING METABOLIC RATE WITH SPECIAL REFERENCE TO PROTEIN METABOLISM

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A curious fact in the estimation of metabolic rate by indirect calorimetry is that the normal 'exact' method of calculation is so cumbersome that the effect of protein metabolism is commonly ignored. Moreover, the total respiratory quotient is used to assign to the oxygen consumed a calorie value which is appropriate only to the non-protein respiratory quotient. This paper describes several ways in which the calculation can be simplified and shows how the effect of protein metabolism can be included with a minimum of trouble. The derivation of the calorie value of 1 litre of oxygen is the first step.

The calorie value of 1 *l. of oxygen*

If K kg.cal. is the calorie value of 1 l. of oxygen and R is the total R.Q., then, using the symbols and numerical values of Table 1, for 1 l. of oxygen consumed we have

$$\text{l. } O_2 \text{ consumed} = x + y + z = 1, \tag{1}$$

$$\text{l. } CO_2 \text{ produced} = R = x + 0{\cdot}802y + 0{\cdot}718z, \tag{2}$$

and

$$\text{kg.cal. liberated} = K = 5{\cdot}047x + 4{\cdot}463y + 4{\cdot}735z. \tag{3}$$

Table 1. Symbols and numerical values used in discussing the metabolism of carbohydrate, protein and fat

	Carbohydrate	Protein	Fat
R.Q.	1	0·802*	0·718†
Kg.cal. per litre of O_2	5·047‡	4·463*	4·735†
Vol. of O_2 metabolizing	x	y	z

* Data of Loewy modified by Lusk (1928).
† Cathcart & Cuthbertson (1931).
‡ Zuntz (1897).

Solving for K by first substituting for x from (1) in (2) and (3) we have

$$R = 1 - 0{\cdot}198y - 0{\cdot}282z, \tag{4}$$

and

$$K = 5{\cdot}047 - 0{\cdot}584y - 0{\cdot}312z, \tag{5}$$

and then substituting for z from (4) in (5) we have

$$K=3\cdot941+1\cdot106R-0\cdot365y. \tag{6}$$

Since R is the total R.Q. and y is the number of litres of oxygen metabolizing protein per litre total oxygen consumption, the term $0\cdot365y$ represents the error in the usual method of calculation, and can be regarded as the correction for protein metabolism. When y is zero, R becomes the non-protein R.Q. and equation (6) then gives the calorie value of 1 l. of oxygen metabolizing carbohydrate and fat, and corresponds to the values in Cathcart & Cuthbertson's table (1931).

The protein correction can be made in several ways. Since 1 g. urinary nitrogen is equivalent to 5·941 l. of oxygen (Lusk, 1928) the correction is $0\cdot365\times5\cdot941=2\cdot17$ kg.cal./g. urinary nitrogen.

Alternatively, if the fraction of the total calorie production due to protein is p, the number of kg.cal. produced by protein metabolism per litre total oxygen consumption is pK, the volume of oxygen consumed is $pK/4\cdot463$ l. and so equation (6) can be rewritten as

$$K=3\cdot941+1\cdot106R-0\cdot365pK/4\cdot463,$$

which, on collecting terms in K, gives

$$K=(3\cdot941+1\cdot106R)/(1+0\cdot082p), \tag{7}$$

or very nearly

$$K=(3\cdot941+1\cdot106R)\,(1-0\cdot082p). \tag{8}$$

The protein correction is equal to a deduction of 1% when $p=0\cdot123$, i.e. when 12·3% of the total calories arise from protein metabolism, and therefore the error in neglecting the effect of protein metabolism is 1% for each 12·3% of the total calories which arise from protein. Appropriate values of p can be used to suit special conditions; but in human metabolism p is usually about 1/8, and then equation (7) reduces very nearly to

$$K=3\cdot9+1\cdot1R. \tag{9}$$

In fact if the percentage of protein calories lies between 10 and 14 the maximum error in using equation (9) is less than 1 in 500.

The equation for the total heat output in a given time is

$$\text{total kg.cal.}=3\cdot941\times\text{l. }O_2\text{ used}+1\cdot106\times\text{l. }CO_2\text{ produced}$$
$$-\text{protein correction (e.g. }2\cdot17\times\text{g. urinary nitrogen)}, \tag{10}$$

or

$$\text{total kg.cal.}=(3\cdot941\times\text{l. }O_2\text{ used}+\text{l. }CO_2\text{ produced})/(1+0\cdot082p), \tag{11}$$

or corresponding to equation (9)

$$\text{total kg.cal.}=3\cdot9\times\text{l. }O_2\text{ used}+1\cdot1\text{ l. }CO_2\text{ produced}. \tag{12}$$

The carbon dioxide production and, in some cases, the oxygen consumption were determined by weight in many of the classical experiments. Indeed such is still the practice in some modern work.

The above formulae are easily modified to suit such data. For example, equation (12) becomes

$$\text{total kg.cal.} = 2{\cdot}729 \times \text{g. } O_2 \text{ used} + 0{\cdot}560 \times \text{g. } CO_2 \text{ produced.} \qquad (13)$$

The calorie value of 1 *l. of expired air*

In ordinary breathing, and also with all open types of respiratory apparatus used for determining energy expenditure, e.g. the Douglas bag, the calorie output is most simply found by multiplying the volume of expired air by the calorie value per litre of expired air.

Corresponding to each litre of expired air let O' l. be the volume of oxygen consumed, C' l. the volume of carbon dioxide produced and K' kg.cal. the heat liberated. Then, using the additional symbols shown in Table 2, we have

$$O' = (N_e O_i - O_e N_i)/100 N_i, \qquad (14)$$

$$C' = (C_e N_i - N_e C_i)/100 N_i, \qquad (15)$$

TABLE 2. Symbols and numerical values used in the description of indirect calorimetry

	CO_2	O_2	N_2
Percentage in inspired air	C_i (0·03)	O_i (20·93)	N_i (79·04)
Percentage in expired air	C_e	O_e	N_e

and, from (10), $K' = 3{\cdot}941 O' + 1{\cdot}106 C'$ - protein correction. Substituting for O' and C' and eliminating N_e by putting $N_e = 100 - C_e - O_e$ we get

$$K' = 1{\cdot}0432 - 0{\cdot}04984 O_e + 0{\cdot}00063 C_e - \text{protein correction},$$

or

$$K' = (1{\cdot}0432 - 0{\cdot}04984 O_e + 0{\cdot}00063 C_e)/(1 + 0{\cdot}082 p). \qquad (16)$$

These equations give the exact value for the heat output; but the small coefficient of C_e indicates that K', i.e. the calorie value of 1 l. of expired air, is practically independent of the percentage of CO_2 in the expired air and, consequently, independent of the R.Q. As a result, the formulae can be simplified by using a mean value of C_e; but, since the variations in C_e are due partly to variations in the rate and depth of breathing and partly to variations in the R.Q., the residual error can be reduced to a minimum by expressing K' in terms of O_e and R.

Heat output in terms of percentage of oxygen in expired air and the R.Q.

One litre of expired air contains $O_e/100$ l. of oxygen. The corresponding volume of inspired air is $1 + O' - C' = 1 + (1 - R) O'$ l. and this contains $\{1 + (1 - R) O'\} O_i/100$ l. of oxygen. The difference is the volume of oxygen consumed, i.e. O' l. Therefore

$$\{1 + (1 - R) O'\} O_i/100 - O_e/100 = O';$$

from which we have $$O' = (O_i - O_e)/\{100 - (1-R)\, O_i\},$$
or $$O' = (O_i - O_e)/(79{\cdot}07 + 20{\cdot}93R).$$

Since the calorie output is equal to the volume of oxygen consumed multiplied by its calorie value per litre, we have from equation (7), omitting the protein correction, $$K' = (O_i - O_e)\,(3{\cdot}941 + 1{\cdot}106R)/(79{\cdot}07 + 20{\cdot}93R).$$

For the range of R, 0·718–1·0, K' lies between 0·05032 $(O_i - O_e)$ and 0·05047 $(O_i - O_e)$, i.e. K' is practically independent of R and in fact with an error of less than 1 in 600 we can write
$$K' = (O_i - O_e)\, 0{\cdot}0504. \tag{17}$$

This equation is applicable when the protein correction is made from the urinary nitrogen. Since, despite its simplicity, it gives the same result as existing methods, the equation can also be used to compare new experimental data with other data in the literature in which the effect of protein metabolism has been neglected. If we use a mean value of O_e, e.g. 16·5, to adjust the coefficient of O_e the calculation can be done mentally. Thus
$$K' = (O_i - O_e)\, 0{\cdot}0504 = 20{\cdot}93 \times 0{\cdot}0504 - 16{\cdot}5 \times 0{\cdot}0004 - 0{\cdot}05O_e,$$
i.e. $$K' = 1{\cdot}048 - 0{\cdot}05O_e. \tag{18}$$

Including the protein correction, equation (17) becomes
$$K' = (O_i - O_e)\, 0{\cdot}0504/(1 + 0{\cdot}082p). \tag{19}$$

If the percentage of calories from protein is 12½, a typical mean value, K' can be read directly from the accompanying nomogram (Fig. 1) or from the simplified formula $$K' = 1{\cdot}046 - 0{\cdot}05O_e. \tag{20}$$

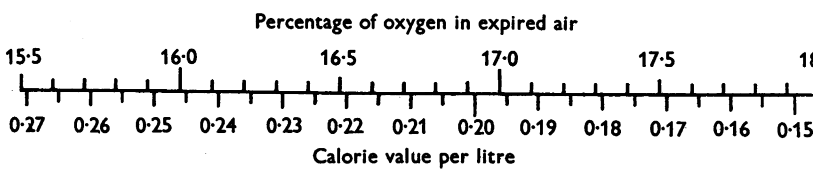

Fig. 1. From the percentage of oxygen in expired air, this nomogram gives the calorie value per litre of expired air. The heat output is given by multiplying the number of litres of expired air by the calorie value per litre. A protein correction is included on the assumption that 10–15% of the total calories arise from protein metabolism.

A physiological curiosity is that when p is 10% equation (19) reduces to $K' = (O_i - O_e)/20$, i.e. the calorie output is five times the apparent oxygen usage.

Normal temperature and pressure and surface area nomograms

In routine calculations much time and labour can be saved by the use of nomograms. The N.T.P. nomogram (Fig. 2) gives the correction factor for reducing the observed volume of a gas saturated with water vapour to the volume measured dry at 0° C. and 760 mm. Hg.

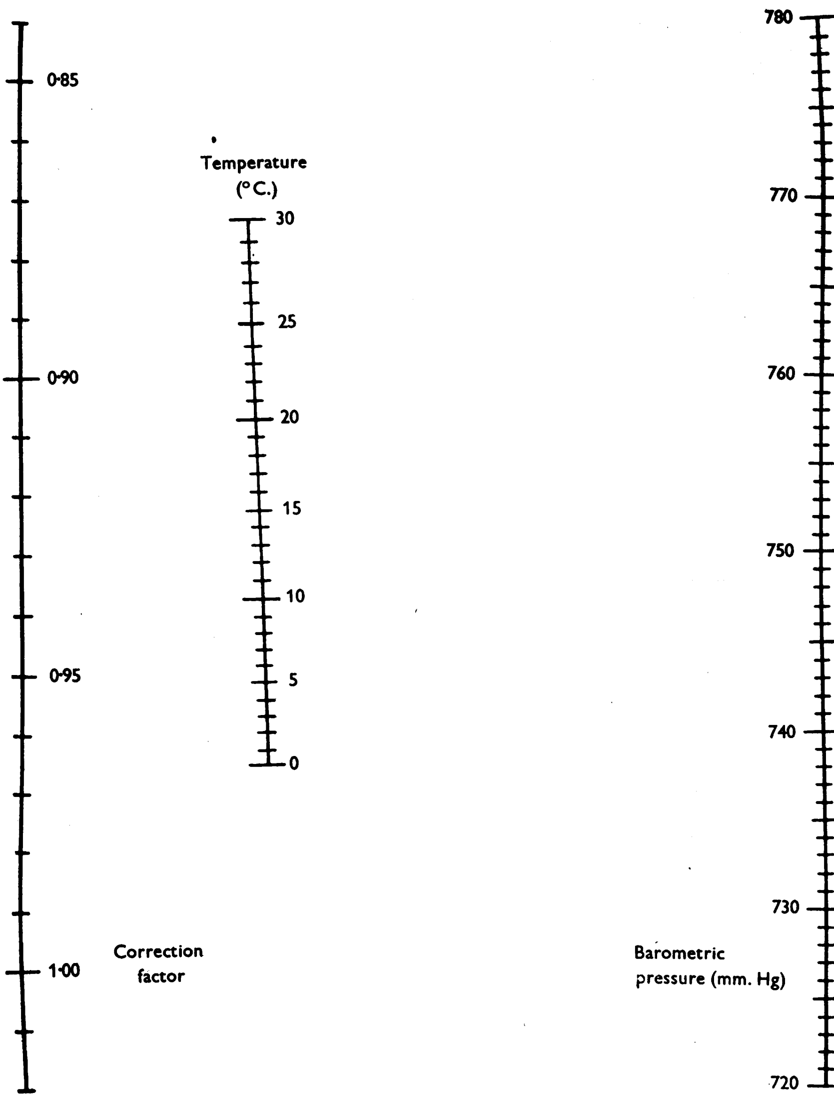

Fig. 2. This nomogram gives the correction factor for finding the dry volume at N.T.P. of a gas saturated with water vapour.

Existing surface area nomograms exemplify a dilemma. If they cover the possible range, the graduations are so crowded that accurate use is difficult or impossible. On the other hand, an open scale results in an inadequate range which is even more annoying. The nomogram of Fig. 3 evaluates the Du Bois formula

$$S = 0{\cdot}007184 \times H^{0{\cdot}725} \times W^{0{\cdot}425},$$

over a considerable range of height and weight, and the weight range can be extended if need be by entering the nomogram with half the observed weight and multiplying the area so found by $2^{0{\cdot}425}$, i.e. 1·343.

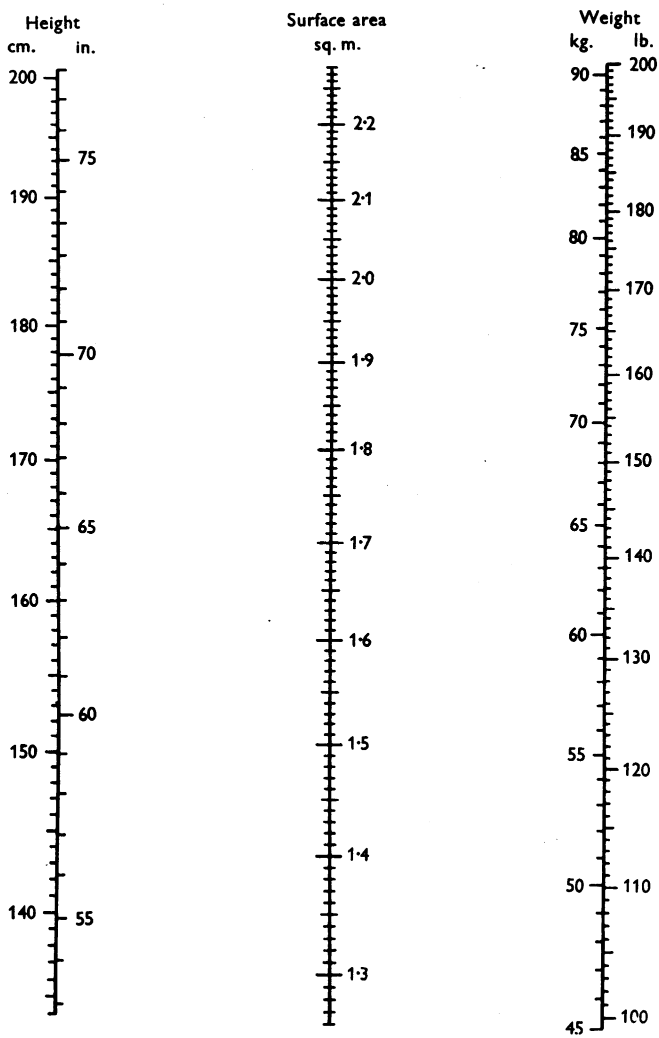

Fig. 3. Surface area nomogram. This evaluates the Du Bois formula. Both British and metric scales for height and weight are incorporated, and the weight range can be extended by entering the nomogram with half the observed weight and multiplying the resulting area by 1·343.

DISCUSSION

The numerical values in the formulae depend on the values of the fundamental data of Table 1. The general solutions are too complex for inclusion here; but other data such as the Zuntz and Schumburg figures for animal fat can readily be substituted.

The equations apply without modification to cases where anabolic processes are occurring, e.g. when fat is being laid down. Corrections similar to the protein correction can be made for other substances, e.g. the combustion of animal fat or of starch along with the deposition of human fat or of glycogen, and these indicate that such reactions should produce a negligible deviation from the present figures. The formula (10), heat output $= 3{\cdot}941 \times$ l. $O_2 + 1{\cdot}106 \times$ l. $CO_2 - 2{\cdot}17 \times$ g. urinary nitrogen, is in effect the theoretical partial regression equation of heat output on oxygen consumption, carbon dioxide production and urinary nitrogen. It shows the relative importance of these factors in indirect calorimetry. The corresponding experimental regression equation would give the closest agreement between direct and indirect calorimetry. It might well show, for example, that the Zuntz figure of 5·047 for the calorie value of oxygen in carbohydrate metabolism, which is very close to the value for starch, is somewhat too high for the post-absorptive state when, presumably, glucose or glycogen is the carbohydrate undergoing metabolism.

The employment of calorie values of oxygen based on the assumption that a fixed percentage of the total calories arise from protein metabolism was suggested by Magnus-Levy (1907). It is realized that for many purposes it is unnecessary and impracticable to make the 'exact' protein correction from the urinary nitrogen. A standard correction on the assumption that protein produces about $12\frac{1}{2}$ % of the total calories has been suggested above. The error introduced, even if the percentage is somewhat different, is practically negligible. Widdowson (1947) has pointed out that the results of dietary surveys in various parts of the world all go to show that the majority of mankind take 10–15 % of their calories in the form of protein. In various environments in different parts of the world Johnson & Kark (1947) found a range of 11–13 %. It does not necessarily follow that there is a similar constancy in the percentage of calories arising from protein metabolism within the duration of any given metabolic determination; but Wishart (1928) found a marked parallelism between daily variations in basal metabolism and variations in the output of nitrogen in the urine.

The finding that the determination of metabolic rate requires only the measurement of the volume of air expired and its oxygen content introduces the possibility of new techniques. The first requirement is a simple, rapid and accurate method of measuring oxygen. Methods which depend on the paramagnetic properties of oxygen are being developed in several laboratories

(British Intelligence Objectives Sub-Committee, 1946; Pauling, Wood & Sturdivant, 1946; Rein, 1943) and already some forms of apparatus have sufficient accuracy to justify their use in metabolic experiments. Some instruments record automatically the oxygen content of a gas stream. This should allow the continuous measurement of metabolic rate over long periods.

In the meantime, however, the majority of laboratories will probably continue to rely on such well-established methods of indirect calorimetry as the Douglas-Haldane technique, and an example showing the simplicity of the calculation by the new method is given in the appendix.

SUMMARY

1. Equations are derived from first principles for the calorie value of a litre of oxygen metabolizing a mixture of carbohydrate, protein and fat. Simple methods for allowing for protein metabolism are described.

2. Heat output similarly can be expressed by such simple formulae as heat output (kg.cal.) $= 3{\cdot}9 \times$ litres oxygen consumed $+ 1{\cdot}1 \times$ litres carbon dioxide produced.

3. In ordinary breathing and in open methods of indirect calorimetry, the heat output is equal to the product of the volume of expired air (ventilation) and the calorie value per litre. This calorie value is almost exactly one-twentieth of the difference in the percentages of oxygen in inspired and expired air.

4. A surface area nomogram with special features and a nomogram for reducing the volume of gases to N.T.P., including the correction for aqueous vapour, complete an extremely simple method of computing metabolic rate.

It is a pleasure to record my indebtedness to Prof. E. P. Cathcart who has done so much in this field of physiology and to Prof. G. H. Bell and Prof. R. C. Garry for their advice and interest in these calculations.

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APPENDIX

Calculation of metabolic rate using Douglas bag method

The following data have been taken for comparative purposes from an article describing the Douglas bag method (Cathcart, 1918).

Volume of air expired in 10 min. 99·75 l., temperature of gas meter 16·8° C., atmospheric pressure 750 mm. Hg. Gas analysis of sample showed oxygen 16·86 % and carbon dioxide 3·54 %. Subject's height 163 cm., weight 50 kg.

From the second nomogram (Fig. 2) the factor for correcting the volume is 0·912 and therefore the volume of dry air at 0° C. and 760 mm. Hg is $99{\cdot}75 \times 0{\cdot}912 = 90{\cdot}97$ l.

From the nomogram of Fig. 1, the calorie value of expired air, including the correction for protein, is 0·203. The calorie output per hour is therefore $0{\cdot}203 \times 90{\cdot}97 \times 6 = 110{\cdot}8$ kg.cal. The surface area, Fig. 3, is 1·52 sq.m. and the metabolic rate is therefore $110{\cdot}8/1{\cdot}52 = 72{\cdot}9$ kg.cal./sq.m./hr.